DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10-20-09 has been entered.

Claims 1-14 remain pending. The claims are being examined as they relate to an intravascular stent having an inner surface comprising cells genetically modified to produce an enzyme capable of catabolizing cholesterol and lipids.

Applicant's arguments filed 9-21-09 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-14 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is drawn to an intravascular stent comprising an inner surface having genetically modified cells that produce an enzyme capable of catabolizing cholesterol and lipids. Claim 11 is drawn to a method of using the stent to treat or prevent obstructive atherosclerotic lesions in coronary and peripheral blood vessels, or prevent restenosis in intra coronaric stents. The sole disclosed use for the claimed invention is for treatment or prophylaxis.

Dichek taught stents comprising genetically modified cells expressing tissue-type plasminogen activator (t-PA) (Circulation, 1989, Vol. 80, pg 1347-1353).

Yuan (Chinese Medical Journal, 2001, Vol. 114, no. 10, pg 1043-1045) coated a metallic stent with adenovirus encoding LacZ immersed in a gelatin solution and a crosslinker.

The art at the time of filing did not teach how to use genetically modified cells encoding an enzyme capable of catabolizing cholesterol and lipids to treat or prevent disease. Nor did the art at the time of filing teach how to use a vector encoding such an enzyme in the absence of genetically modified cells (direct injection of a vector or plasmid) to treat or prevent disease so that one of skill could guess how to use genetically modified cells encoding such and enzyme. Accordingly, it was unpredictable how to target cells of interest using genetically modified cells expressing an enzyme capable of catabolizing cholesterol and lipids to treat or prevent disease.

The specification teaches immobilizing cells on a stent having an underlayer of nitrogen (pg 5-6, Example 1). Example 2 teaches transfecting umbilical vein endothelial

cell line with an AAV vector encoding lipoprotein lipase (LPL) and seeding the cells onto a stent.

The specification does not teach where to insert the stent, the amount of LPL expressed, the amount of LPL required to treat or prevent disease or how to target the LPL to the tissues of interest such that disease is treated or prevented. Without such guidance, the specification fails to overcome the unpredictability in the art to use the stent comprising genetically modified cells expressing LPL to treat or prevent disease. Accordingly, the specification fails to enable those of skill to use the claimed invention for its sole disclosed use – therapy or prophylaxis.

Applicants argue each part of the product in claim 1 must merely be taught in the specification or known in the art to meet the requirements for enablement. Applicants' argument is not persuasive. The standard for enablement requires that applicants must also provide adequate guidance for those of skill to use the product. In this case, the specification taken with the art at the time of filing and the art established unpredictability of gene therapy fails to adequately teach those of skill how to use the invention for its sole disclosed use - treatment or prophylaxis. Applicants have not pointed to any disclosed use for the invention of claim 1 other than therapy or prophylaxis.

Applicants argue the Examiner's statement regarding the state of the art is an indication of the novelty of the treatment in claim 11. Applicants' argument is moot because the rejection at hand is enablement, not novelty.

Applicants argue the specification provides adequate guidance to use the invention of claim 1 for therapy or prophylaxis and to perform the method of claim 11 to treat or prevent obstructive atherosclerotic lesions in coronary and peripheral blood vessels or prevent restenosis in intra coronaric stents. Applicants argue they teach LPL can be put into adenovirus which is then put into human normal umbilical vein endothelial cells (HUVEC) as described on pg 7-9. Applicants point to Exhibits D5-7 for support of making cells encoding LPL. Applicants' arguments are not persuasive. D5 is the abstract of Russell (Nature Genetics, 1998, Vol. 18, pg 325-330). D6 is the abstract of Lewis (Human Gene Therapy, Jul. 1995, Vol. 6, No. 7, pg 853-863). D7 is the abstract of Poirier (Biochem. and Biophysical Res. Comm., 2000, Vol. 270, No. 3, pg 997-1011). Applicants' arguments are not persuasive. The enablement rejection is not based on how to make the cells comprising an adenoviral vector encoding LPL as described on pg 7-9. The rejection is based on how to use such cells in a stent as in claim 1 for its sole disclosed use - treatment or prophylaxis. Furthermore, the claims are not limited to a stent comprising HUVEC comprising adenovirus encoding LPL. Finally, and most importantly, the specification taken with the art at the time of filing including Russell, Lewis and Poirier, do not provide adequate guidance that such cells treat or prevent disease given the unpredictability of gene therapy.

Applicants point to pg 5, line 22-25, which refers to the stent as "intravascular" used for treatment or prevention of obstructive atherosclerotic lesions in the coronary and peripheral blood vessels. Applicants point to pg 2, line 4, which states the stent can be put into a vascular lumen. Applicants point to Exhibits D1-2. D1 is the abstract of

Goy (Am. J. Cardiol., 1991, Vol. 67, No. 7, pg 569-572). D2 is the abstract of Hildick-Smith (J. Interv. Cardiol., 2001, Vol. 14, No. 4, pg 439-442). Applicants' arguments are not persuasive. It was well known at the time of filing that stents were put into vascular lumens; however, applicants fail to teach where within the vascular system those of skill have to put the stent to treat or prevent obstructive atherosclerotic lesions in the coronary and peripheral blood vessels. Assuming the stent has been put at the location of a lesion, the specification fails to teach the stent produces adequate LPL to treat or prevent disease (it is noted however, that the specification does not teach inserting the stent at the location of the lesion and the claims are not limited to inserting the stent at the location of the lesion). It is unclear how much LPL is expressed in the stents of the invention, how far the LPL would go and whether the amounts of LPL expressed and the amount of targeting possible were enough to treat or prevent disease. These parameters are essential to use the stent claimed to treat or prevent disease. It would have required those of skill undue experimentation to determine such parameters especially given the state of gene therapy in which it was unpredictable whether the expression levels and targeting of gene therapy would treat or prevent disease. Without such guidance, the specification fails to overcome the unpredictability in the art to use the stent claimed to treat or prevent disease.

Applicants argue the amount of LPL required was known at the time of filing as described by Exhibit D8. D8 is the abstract of Ruge, Eur. J. Clin. Invest, Dec. 2001, Vol. 31, No. 12, pg 1040-1047). Applicants' argument is not persuasive. It is not readily apparent that applicants' cells described on pg 7-9 express therapeutic levels of LPL.

Applicants argue the LPL is targeted to tissues of interest simply by providing LPL on the inner surface of a stent and inserting this stent in the desired location". Applicants' argument is not persuasive. The specification does not teach the "desired location" that allows adequate LPL to target the tissue of interest or the amount of LPL expression required to treat or prevent any lesion or prevent restenosis.

Written Description

Claims 1-14 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an intravascular stent comprising an inner surface having genetically modified cells that produce an enzyme capable of catabolizing cholesterol and lipids. Claim 11 is drawn to a method of using the stent to treat or prevent obstructive atherosclerotic lesions in coronary and peripheral blood vessels, or prevent restenosis in intra coronaric stents.

The phrase enzyme "capable of catabolizing cholesterol and lipids" lacks written description. The phrase is mentioned on pg 4, but the only enzyme disclosed in the specification or the prior art of record that catabolizes cholesterol and lipids is lipoprotein lipase (LPL). Therefore, the claims should be limited to LPL.

Applicants argue the written description is misplaced because it typically applies to new matter. Applicants' argument is not persuasive. "New matter" rejections relate

to amendments that fail to be adequate described in the specification as originally filed; such rejections also come under the heading of "Written Description." In this case, applicants' disclosure fails to adequately describe the genus of enzymes "capable of catabolizing cholesterol and lipids". One species (LPL) of the genus (enzymes capable of catabolizing cholesterol and lipids) fails to meet the burden of "written description." Therefore, the claims should be limited to LPL. Applicants' arguments fail to address the fact that the specification and the art at the time of filing do not teach any other enzymes in the genus claimed.

The art at the time of filing did not reasonably teach or suggest a stent comprising cells genetically modified to produce an enzyme capable of catabolizing cholesterol and lipids as claimed. In particular, in vivo or ex vivo LPL gene therapy was not adequately taught or suggested in the art at the time of filing. Accordingly, those of ordinary skill would not have reasonably combined stent technology with cells genetically modified to produce an enzyme capable of catabolizing cholesterol and lipids as claimed.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner